



Institute for In Vitro Sciences, Inc.



## ICCVAM Eye Tests Comments to the Expert Panel II.

Presented By

**Institute for In Vitro Sciences**

January 12, 2005

# Items Addressed

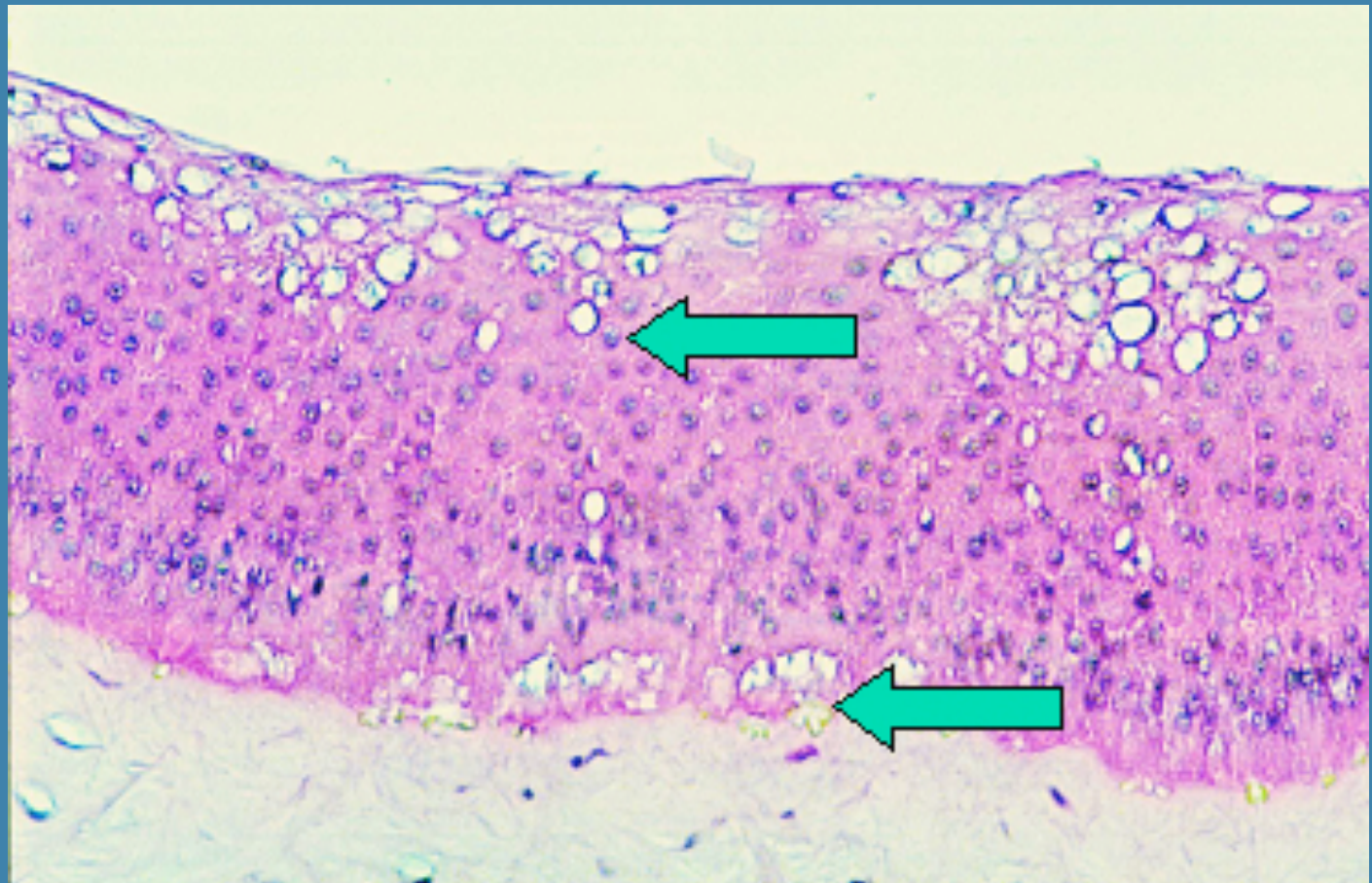
- How does the addition of histological evaluation affect the performance statistics ?
- Accuracy Vs. Concordance
- Statistical evaluation of new test methods

# BCOP Performance in HO/EC Study - Addition of Histology

Chemical	EU	EPA	Rabbit MAS	MMAS	IVS HO/EC	Histology
BAK 10%	R41	1			136.4	
BAK 5%	R41	1			128.6	
BAK 1%	R36/R41	1			88.8	
Benzyol - L - Tartaric Acid	R41	1			169.6	
Captan 90	R41	1	63, 81, 105	83	43.8	
CPB 6%	R41	?			71.2	
CPB 10%	R41	1			72.2	
Chlorhexidine	R41	1			114	
Cyclohexanol	R41	1	2/4 cleared by D10, 1/4 by D14		60?	
2,2-dimethylbutanoic acid	R41	1			112	
2,5 dimethylhexanediol	R41	1	22, 31, 32	28.3	20.6	
Imidazole	R41	1			112.6	
1-naphthalene acetic acid	R41	1			149.2	
1-naphthalene acetic acid, Na salt	R41	1			78	
Promethazine HCl	R41	1			121.4	
Pyridine	R41	1			148	
Quinacrine	R41	1			1.4	Severe
NaOH 10%	R41	1			271.8	
SLS 15%	R36	1			63.6	
Sodium oxalate	R41	1			14.3	Severe
Sodium Perborate	R41	1			97.2	
TCA 30%	R41	1			264.2	
					Red = Underestimate	

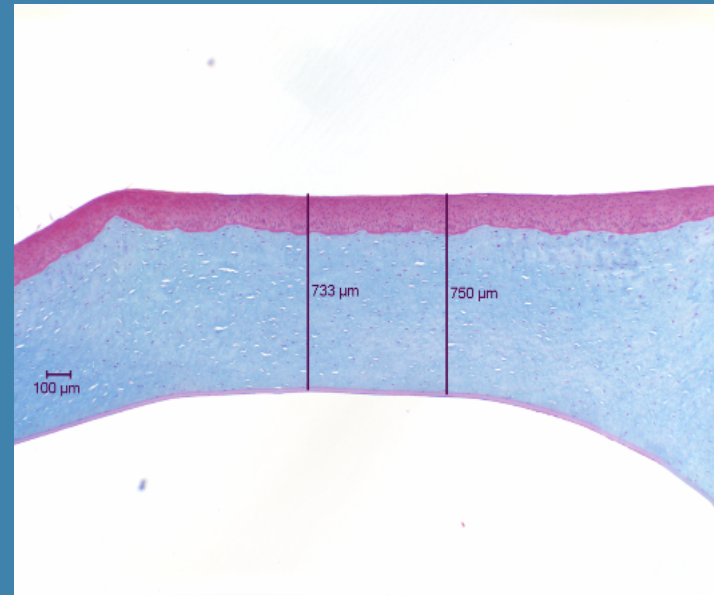
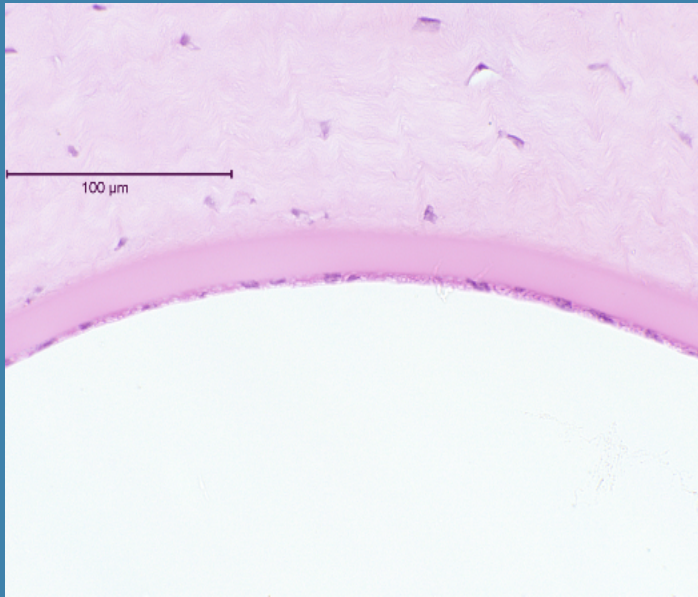
# Histology of EC/HO Materials

Sodium  
Oxalate

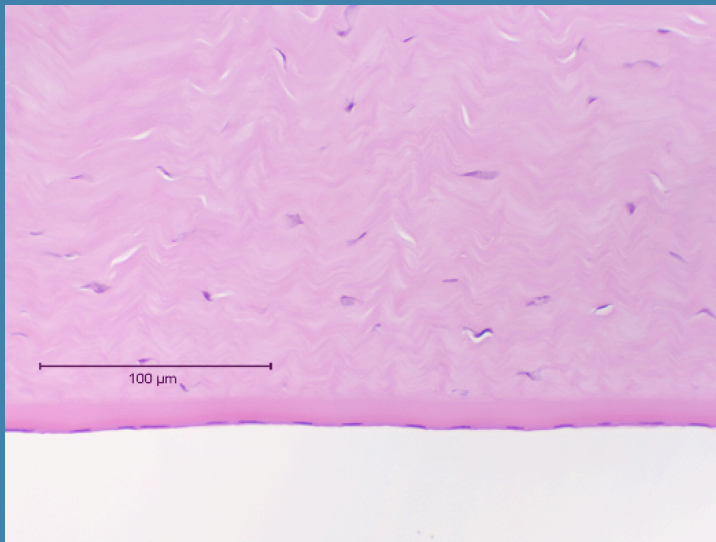


# Quinacrine

Quinacrine



Control



Depth of injury from the quinacrine exposure extended through the endothelial layer but did not lead to any appreciable corneal swelling

# Change of Statistics with Addition of Histology

Evaluation of R41 by IVS only				Evaluation of R41 by IVS + Histology			
Sensitivity = 17/21				Sensitivity = 19/21			
Sensitivity = 81%				Sensitivity = 90%			
Evaluation of Category 1 by IVS only				Evaluation of Cat 1 by IVS + Histology			
Sensitivity = 17/21				Sensitivity = 19/21			
Sensitivity = 81%				Sensitivity = 90%			

# Accuracy Vs. Concordance

- “Accuracy expresses the closeness of test results to a “true” value” or accepted reference value - paraphrased from ASTM Standard Practice
- To my mind an accepted reference value must be of high quality, e.g. a precise analytical measurement.
- Many of us think the “true” value is the human result, with the animal only an imprecise surrogate.
- What we are trying to convey with the statistics presented today is the performance of the in vitro method relative to the rabbit (for eye irritation). We are creating a set of “performance statistics” to describe this.
- ...and within the performance statistics are measures of concordance with the rabbit test results.

# Important Reference on the Use of Statistics to Understand Performance

Feinstein, AR. (1975) Clinical Biostatistics. XXXI. On the sensitivity, specificity, and discrimination of diagnostic tests. Clin. Pharmacol. Therap. 17:104-116.

Dr. Feinstein gives an excellent discussion concerning the need of physicians (or toxicologists) to use a set of statistics which help them understand the meaning of a test result (how predictive is the result?). This is predictive value, quite different from sensitivity and specificity. Both statistics, sadly, are highly influenced by prevalence - the percentage of positive materials (or diseased patients) in the general population or in the validation set.

